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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,026	06/11/2007	Bror Morein	ALBI-41848	6185

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,026	MOREIN ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *3,11,16,17 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10,12-15,18 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/6/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-26 are pending in the application.

2. In the prior action, mailed on August 6, 2009, claims 1-26 were pending in the application; with claims 3, 11, 16, 17, and 19 withdrawn from consideration; and claims 1, 2, 4-10, 12-15, 18, and 20-26 under consideration are rejected.

3. In the Response of November 6, 2009, the Applicant amended claim 26.

4. Claims 1, 2, 4-10, 12-15, 18, and 20-26 are under consideration.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on November 6, 2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Objections

6. **(Prior Objection- Withdrawn)** Claim 26 was objected to because of the following informalities: it appears that the claim would more clearly describe the claimed invention by indicating that the composition "provides for enhanced immunogenicity of the live micro-organism in a host." In view of the amendment of the claim, the objection is withdrawn.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. **(Prior Rejection- Maintained)** Claims 1, 2, 4, 9, 10, 12, 15, 18, and 24-26 were rejected under 35 U.S.C. 103(a) as being unpatentable over Van Woensel et al. (U.S. 5,925,359) in combination with the teachings of Morein et al., (U.S. 5,679,354).

The Applicant provides three general arguments in traversal of the rejection.

First, the Applicant argues that the teachings of Van Woensel in combination with Morein would not have rendered obvious the claimed methods or compositions. The Applicant provides three assertions in support of the argument. Applicant first asserts that Van Woensel lack credibility in the suggestion for the use of an adjuvant with a live vaccine on the basis that adjuvants in general, and saponins in specific, would not have been desirable with a live vaccines. With respect to the arguments presented both in the attorney's remarks and in the Morein declaration (each of which substantially mirrors the other) it is noted that none of the evidence presented specifically provides any teaching away from the combination of an iscom with a live vaccine. The teachings in the art indicate that such is generally not done, but fails to provide any teaching that specifically criticizes, discredits, or otherwise discourages the combination of an iscom with a live vaccine.

With respect to adjuvants generally, it is noted that even the excerpts relied on by the Applicant in the remarks (page 11 of the response) indicate that the use of an adjuvant with a live vaccine was not done, but was also not excluded by the teachings in the art.

With respect to the antimicrobial nature of the saponins, it is noted that these teachings are made relative to the saponins themselves. However, an iscom is not a pure saponin, but is a particle wherein the saponin is combined with cholesterol. While Morein indicates that the saponins are known to have membrane-permeabilizing activity, other teachings in the art (see e.g. Lipford et al., Vaccine 12:73-80) indicate that this activity appears to specifically be associated with the ability of saponins to intercalate with cholesterol containing membranes. Page 78, left column. In addition the teachings in the art appear to indicate that the detergent activities (such as membrane permeabilization) of saponins appear to be absent when incorporated in to iscoms. Gupta et al., Vaccine 11: 293-306, at 299(right column). Thus, while those of ordinary skill in the art may have considered saponins themselves to be inappropriate for use as adjuvants in live vaccines, in view of the above teachings, those of ordinary skill in the art would not have expected the same incompatability between the use of isoms and live vaccines.

In view of the above, while the teachings of Van Woensel may not have been credible with respect to the use of a pure saponin with a live virus vaccine, the reference does not teach such a combination. Because the reference suggests the combination of the live virus with an iscom adjuvant, and in view of the knowledge and teachings in the art regarding saponins and iscoms as indicated above, Applicant's arguments regarding the credibility of Van Woensel are not found persuasive with respect to the combination of a live virus with an iscom adjuvant.

The second assertion by the Applicant is based upon the assertion in the Morein declaration that, while the reference suggests the combination of a whole virus with an iscom,

the inventors (including Morein) of that reference did not "intend" that the iscoms would be used with live vaccines. While this may be the case, the teachings of a prior art reference are applied as for what they would have taught and suggested to those of ordinary skill in the art, and not necessarily for what the authors "intended" to convey. From the teachings of the cited references, there would have been adequate suggestion in the art that iscom based adjuvants could be used as adjuvants to live vaccines. Thus, the Applicant's assertion as to what was intended by the authors of the Morein reference is not found persuasive.

Applicant's third assertion is an assertion that the combined teachings of the Van Woensel and Morein references fail to cure the deficiencies of the references individually. This argument is not found persuasive for at least the reasons above (i.e. the asserted deficiencies of the individual references are not found persuasive).

Moreover, it is also noted that the rejection is not solely dependent on the use of the iscoms as direct adjuvants for the live vaccines. Rather, Van Woensel teaches the use of iscoms as adjuvants for subunit or inactivated vaccines that may be used in combination with the live viruses. See e.g., pages 4-5 of the prior action. Thus, the combined teachings in the art render obvious the use of iscoms in the same composition as live virus vaccines, whether as adjuvants for the live virus, or primarily as adjuvants for incorporated non-live antigens (with only secondary activity as an adjuvant for the included live virus).

For these reasons, Applicant's first basis of traversal is not found persuasive.

Applicant's second argument in traversal is that there would have been no reasonable expectation of success in the use of the iscoms as adjuvants for the compositions as claimed in view of the multiple and potentially deleterious responses that iscoms may induce. The arguments are directed both to potentially negative results in the host to whom the vaccine is to be administered, and to the live vaccine included in the composition. The arguments are not found persuasive.

With respect to the response of the host to the iscoms, while the art indicates that the iscoms may trigger multiple responses, the teachings in the art nowhere indicate that such particles are inappropriate adjuvants due to such responses. Rather, it is merely a warning to those in the art that caution should be used when using such adjuvants. However, as similar precautions are required generally when using adjuvants (see e.g., Gupta, teaching the need for balancing adjuvant side effects and benefits for vaccine adjuvanticity), such is not considered a teaching away from the use of such constructs as vaccine adjuvants.

Moreover, the fact that the iscoms may induce a range of responses is also not found to affect the expectation that the iscoms would be suitable adjuvants. Rather, this adjuvant activity merely indicates that iscoms would have been expected to prime the immune system to induce multiple immune responses against the target antigen. The fact that certain extraneous or non-essential responses would also be induced is not a demonstration that the adjuvant activity as a whole would be extraneous.

With respect to the uncertainty regarding IL-12 responses, regardless of the expectation regarding such responses, those of ordinary skill in the art would have had some expectation that the iscom would provide some benefit as an adjuvant to the compositions suggested by the

teachings of the applied references. While the precise effects on IL-12 production may not have been known, this is not essential to a finding that there would have been a reasonable expectation of success in the use of a known adjuvant as an adjuvant in a suggested vaccine composition.

The Applicant's arguments with respect to the use of the iscom as an adjuvant are therefore not found persuasive.

With respect to the potential harm to the live vaccine, it is first noted that the negative attributes of saponins relative to live vaccines is not necessarily present with respect to iscoms. Moreover, the Applicant themselves noted on page 19 of the response that the teachings in the art suggest the reconstitution of a live vaccine immediately prior to use. Thus, if those in the art did fear for the inactivation of the live antigens by the iscoms, it would similarly have been obvious to those in the art to limit such effects (if any) through the combination of the iscoms and viruses immediately prior to use.

For these reasons Applicants second set of arguments are also not found persuasive.

Thirdly and finally, the Applicant asserts unexpected results of the claimed inventions. The Applicant asserts unexpected results in terms of an unexpected ability of the iscom containing compositions to not decrease replication of the micro-organism and to increase the antibody titer against the live microorganisms.

With respect to the ability to not decrease microorganism replication, it is noted that this assertion of unexpected results is based on the fact that it was known that saponins have anti-microbial and antiviral activity. However, as was indicated above, there would have been reason in the art to expect that saponin adjuvants wherein the saponin is incorporated into iscoms would

not have similar anti-microbial activity. Thus, the Applicant has not demonstrated an unexpected effect by showing that iscoms, in contrast to saponins, would not decrease viral replication.

With respect to the ability of the iscom adjuvant compositions to increase antibody production relative to an un-adjuvanted composition, such would have been expected by the very nature of the iscom as an adjuvant. I.e., one of ordinary skill in the art would have expected an adjuvant generally, and an iscom adjuvant in specific, to be capable of increasing the antibody response to a composition comprising such an adjuvant relative to one not comprising the adjuvant.

For these reasons, neither of the assertions of unexpected results is found persuasive. The rejection is therefore maintained for the reasons above, and the reasons of record.

9. **(Prior Rejection- Maintained)** Claims 5-8, 13, 14, and 20-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Van Woensel and Morein as applied above, and further in view of Cox et al. (WO 96/11711). The Applicant traverses the rejection on the same basis asserted with respect to the rejection over Van Woesel and Morein above. The arguments are not found persuasive for the reasons above. The rejection is therefore maintained for the reasons above, and the reasons of record.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648